REMARKS

I. Status of the Claims

Claims 8-15 and 17-18 are currently pending, with claims 17 and 18 withdrawn from consideration as being directed to a non-elected invention. Upon entry of this amendment, claims 11-15 are amended without prejudice or disclaimer. Applicants reserve the right to reintroduce the unamended claims in this or another application. Claims 8-15 and 17-18 are thus pending following entry of this amendment.

II. Information Disclosure Statement

Applicants thank the Examiner for considering the documents listed in the information disclosure statement filed on September 29, 2003. It is noted, however, that Applicants did not receive a marked-off copy of page 1 of this statement, but only page 2. It is requested that a marked-off copy of page 1 be included with the next communication from the Office to confirm consideration of the documents listed on this page.

III. Objections to the Specification

Paragraph 0065 has been updated to include the PCT application number and corresponding publication number for the PCT application referred to in this paragraph.

The references in paragraph 0074 to Figure 2 have been deleted, as has the reference to a table in paragraph 00189.

The Office Action also objects to the reference to SDS-PAGE gel result in paragraph 00189 in the absence of a figure that shows the results. It is submitted, however, that it is sufficient simply to describe the results that were obtained; a figure is not required in this instance because those of ordinary skill in the art can understand the results of this particular from the description of the results of the experiment without reference to a figure that shows the results.

IV. Claim Rejections under 35 U.S.C. §112

A. Written Description

Claims 8-10 and 12-15 are rejected under 35 U.S.C. §112, first paragraph for an alleged failure to reasonably convey that the inventors were in possession of the currently claimed invention as of the effective filing date of the application. For the reasons that follow, Applicants respectfully disagree.

Guidance for considering whether a claim satisfies the written description requirement is set forth in the Written Description Guidelines (Guidelines), published on January 5, 2001 in the Federal Register, vol. 66, pages 1099-1111 (the Interim Guidelines referred to in the Office Action are superseded by these later-published Guidelines).

Under the Guidelines, a claim directed to a genus (e.g., independent claim 8) can satisfy the written description requirement by, for example, disclosing "relevant identifying characteristics" (Id. at page 1106). Examples of "relevant identifying characteristics" are said to include: (1) structures or other chemical or physical properties, (2) functional characteristics coupled with a known or disclosed correlation between structure and function, or (3) combinations of such identifying characteristics.

The specification and claims satisfy the written description requirement by disclosing several relevant identifying characteristics. For example, claim 8 defines the proteins of the presently claimed invention as having greater than 90% sequence identity to SEQ ID NOs:2, 4, 6, 8 or 10, thereby satisfying the chemical or structural criterion set forth in (1). Moreover, claim 8 also satisfies criterion (2) by defining the currently claimed proteins as having microtubule-stimulated ATPase activity (functional activity), which the specification states are proteins that generally have greater than 70% sequence identity to SEQ ID NOs:2, 4, 6, 8, or 10 (see, e.g., paragraph [0067]) and which claim 8 indicates are proteins that have at least 90% sequence identity to the foregoing sequences. So for both these reasons the specification and claims clearly satisfy the written description requirements as set forth in the Guidelines.

Furthermore, the position taken in the Office Action is contrary to the conclusion reached in Example 14 of the "Synopsis of Application of Written Description Guidelines" (Synopsis), which provides examples of the type of analysis used by the Office in evaluating

compliance with the written description requirement. Example 14 is directly analogous to the current claims. The claim in Example 14 reads as follows:

A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B.

Because the claim defines the genus in functional terms that are related to a disclosed correlation between structure and function (one of the Guideline criteria listed above), the Synopsis concludes that the disclosure meets the written description requirements with respect to this exemplary claim. Current claim 8 is in the same general format as this claim (i.e., it too links functional characteristics to structural characteristics) and, as noted above, this relationship is fully supported by the specification (see, e.g., paragraph [0067]). So by analogy, current claim 8 satisfies the written description requirements for the same reasons as the exemplary claim presented in Example 14 of the Synopsis.

For all the foregoing reasons, it is submitted that the present claims satisfy the written description requirement and that this rejection should be withdrawn.

B. Enablement

Claims 8-10 and 11-15 are rejected because the Office Action contends that it would require undue experimentation to practice the currently claimed invention. The Office Action cites a number of references for the proposition that protein chemistry is highly unpredictable and that even minor changes can dramatically affect the activity of the protein. It is thus noted that the effect of sequence alterations "cannot be *predicted a priori* and must be determined empirically on a case-by-case basis" (Office Action at page 6; emphasis added). It is concluded that undue experimentation would be required to practice the claimed invention. The Office Action thus appears to take the position that undue experimentation is required to practice the invention unless one can *predict* based on the disclosure of the application which variants of the listed sequences will be active.

In response, it is submitted that the Office is applying the wrong standard to determine whether the enablement standard is satisfied, and secondly that the application provides sufficient guidance to guide one of ordinary skill in the art to make appropriate variants.

In addressing when experimentation is undue experimentation, the Federal Circuit has stated:

> [E]xperimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art...*The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.* (*In re Wands* 8 USPQ2d 1400, 858 F.2d 731, 737 (Fed. Cir. 1988) (emphasis added)).

Thus, experimentation is not deemed to be undue according to the Federal Circuit if EITHER of two requirements are satisfied: (1) the experimentation is routine, OR (2) the specification provides reasonable guidance in the direction the experimentation should proceed. Contrary to the apparent position taken in the Office Action, *predictive* ability is not required.

Although only *one* of these criteria need be satisfied, it is submitted that the specification satisfies *both*. With respect to the first criterion, the issue thus is whether one of ordinary skill in the art can *routinely* (a) make a protein variant that has 90% sequence identity to SEQ ID NOs:2, 4, 6, 8 or 10, and (b) determine whether such variants have microtubule-stimulated ATPase activity. It is submitted that the answer to both of these inquiries is "yes."

With respect to issue (a) it is first noted that the application lists a number of references that discuss conventional methods for altering the sequence of proteins (see, e.g., paragraphs [0035] and [0076]-[0079]). Moreover, a copy of a section from the well-known 1989 Creighton reference on proteins is enclosed. This section states that "[p]resent day site directed

mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions" ("Protein Structure: A Practical Approach" (Creighton, T.E., Ed.) IRL Press, 1989, pp. 184-185). Since this edition of Creighton significantly predates the priority date of the instant application, those of ordinary skill in the art could have readily prepared variants such as recited in the current claims as of the filing date of the application. With respect to issue (b), the specification describes a variety of assays that can be routinely utilized to assay for microtubule-stimulated ATPase activity (see, e.g., paragraphs [00135] and [00137] and [00138]).

So one of ordinary skill in the art could make variant proteins that that have 90% sequence identity with SEQ ID NOs:2, 4, 6, 8 and 10 using techniques that Creighton says were *routine* in the art. The proteins encoded by these nucleic acids could then be *routinely* analyzed for microtubule-stimulated ATPase activity using any of the assays recited in the application. This is all that the law requires to satisfy the requirements of criterion (1) listed above. For this reason alone, it is submitted that the current claims are thus enabled.

Nonetheless, it is also submitted that the specification also satisfies criterion (2), because the specification provides guidance on the direction that experimentation should proceed to obtain proteins with the recited sequence and activity characteristics. The specification, for instance, teaches that in preparing variants that generally a relatively few amino acids should be modified to minimize alteration of protein activity (see, e.g., paragraphs [0036] and [0037]). It further lists conservative amino acid substitutions that were generally known not to affect protein activity adversely (see, e.g., paragraph [0038]). The specification also cites to an earlier edition of the Creighton reference for further guidance on this issue, thus providing evidence that information on conservative substitutions were known as of the effective date (see paragraph [0038]).

The specification also teaches that the claimed PfKinI-1 proteins are members of the KinI subfamily that is part of the larger kinesin family of proteins (see, e.g., paragraph [0004]), that the PfKinI-1 proteins are homologous with HsKinI-3 (see, e.g., paragraph [0065]), and that some PfKinI-1 proteins include a motor domain, which is a common feature of the kinesin family of proteins (see, e.g., paragraph [0068]). Those of ordinary skill in the art would

thus know that one logical approach for obtaining active variants of SEQ ID NOs:2, 4, 6, 8 and 10 that have microtubule-stimulated activity would involve first identifying conserved and non-conserved regions between the listed protein sequences and related members of the KinI family. This could be readily done using sequence comparison algorithms such as those listed in the specification (see, e.g., paragraphs [0029]-[0031]). Skilled practitioners would further recognize that likely candidates for alteration that would still yield an active protein would be those amino acids in non-conserved regions, as such regions by definition appear to tolerate differences in sequence. It is thus submitted that the guidance in the specification coupled with the general knowledge in the art would have enabled one of ordinary skill to identify appropriate residues for modification.

So although the law requires only that criterion (1) OR (2) listed above be satisfied for the claims to be enabled, it is submitted for all the foregoing reasons that the application in fact satisfies BOTH. Accordingly, it is requested that the enablement rejection also be withdrawn.

V. Claim Rejections under 35 U.S.C. §102(b)

Claims 11-15 are rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 4,767,622 to Ristic et al. ("Ristic"). Ristic is said to discuss the isolation of certain proteins characterized by 1) having a molecular weight of between 35-85 kDa, and 2) being water-soluble proteins that are found secreted into the culture medium or present in a wash solution after infected cells have been rinsed in the wash solution. The Office Action acknowledges that Ristic includes no discussion of proteins that have sequence and activity characteristics recited in the current claims. It is nonetheless argued that these are simply inherent properties of proteins discussed in Ristic.

It is submitted that Ristic fails to anticipate the currently pending claims for at least two reasons. First, to reject a claim as being anticipated under the inherency doctrine, the Patent Office must overcome a substantial burden. Specifically, the Federal Circuit has said:

> To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' (MPEP 2112; citing In re Robinson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-1951 (Fed. Cir. 1999) (emphasis added).

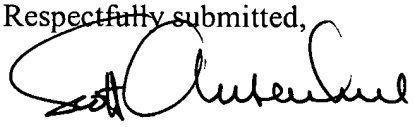
Here the Patent Office has not provided any justification whatsoever to conclude that the proteins discussed in Ristic *necessarily* have the characteristics of the currently claimed proteins.

Secondly, as noted above, the currently claimed proteins are members of the KinI-1 family of proteins (see, e.g., paragraphs [0004] and [0065]). These proteins are involved in various microtubule processes in the *nucleus* of the cell (see, e.g., paragraphs [0004] and [0066]). As such these proteins would *not* be expected to be secreted outside the cell or rinsed from the cells as is the case with the proteins discussed in Ristic.

So for both these reasons it is submitted that Ristic fails to anticipate the pending claims. It is thus accordingly requested that this rejection be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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